UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 25 1993

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM **Expedite**

SUBJECT: **SULFURYL FLUORIDE.** ID #078003. Review of Study Protocol for Evaluation of Short-Term Inhalation Neurotoxicity in Rats (to Fulfill Guideline 81-8 Requirement).

PC No.: 078003
Tox. Chem. No.: 816A
DP Barcode: D186112
Submission No.: S432585

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THRU: Marion P. Copley, D.V.M., D.A.B.T., Section Head
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CONCLUSIONS:

TB-I considers the overall study design adequate for fulfilling the data requirements requested for short-term inhalation neurotoxicity of sulfuryl fluoride (modified 81-8), with the exception of the points outlined below. The protocol provided a very detailed and complete outline of study design and materials and methods to be used. TB-I has no objection to testing in 3 subgroups of 4 animals/dose group, nor to use of females only. Choices of doses (0, 100 and 300 ppm), number of animals per treatment group (12 females) and treatment duration (2 days x 6 hrs/day) appear adequate. Limiting of electrophysiology testing to those parameters which were significantly affected by treatment in the 90-day study was previously discussed with TB-I.

The following comments address specific points in the protocol:

1. Functional observational batteries and electrophysiological testing are to be conducted pretest and on the day following the second day of treatment according to the protocol. However, by testing on the day following treatment, peak effect may

have been lost. If it cannot be determined that the peak effect is still present on the day following treatment, the animals should be tested within 8 hrs of treatment. TB-I also asks that for each animal the time interval between termination of treatment and initiation of testing, and also the duration of testing, be noted in the study report.

2. It is recommended that historical control data (preferably negative and positive) should be provided to aid interpretation of the results.

3. It is recommended that positive control animals be run along with treated and negative control animals.

4. Motor activity testing should be conducted along with the electrophysiological and functional observational testing, as part of the requirements for acute neurotoxicity testing <u>unless</u> it can be shown from previous studies that motor activity is only affected at doses significantly higher than those affecting electrophysiological or functional parameters.

5. Recovery testing should be conducted on animals in which treatment-related effects are observed, including at 7 and 14 days post-treatment (and at 1 month, if necessary).

<u>ACTION REQUESTED</u>:

On December 9, 1992 DowElanco submitted a draft protocol entitled "Vikane: Electrodiagnostic and functional observational battery evaluation of nervous system effects from short-term exposure" and requested evaluation by HED (letter from Jeffrey D. Pinkham, Product Registration Manager). An expedited review was requested in order that the study be initiated on the planned date of Feb. 1, 1993. This data was requested by TB-I as part of a recent Data-Call In for sulfuryl fluoride (memos from L. Hansen to L. Rossi, dated 7-31-92 and 10-8-92) to provide a reasonable estimate of short-term exposure risk using the most sensitive toxicity endpoint (functional neurotoxicity). Some experimental parameters usually part of Guideline 81-8 are not required (or have been modified) because (1) information from previous studies in rats, taken together with data from the proposed study, should provide sufficient data for determination of acute neurotoxicity risk and (2) the major intent of this study is to determine a reasonable NOEL for neurotoxicity for short-term exposure.